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ART UNIT	**PAPER NUMBER**
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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/724,000	Applicant(s) POLVERINO ET AL.	
	Examiner Stephen L. Rawlings, Ph.D.	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,18-36 and 40-62* is/are pending in the application.

4a) Of the above claim(s) *1-8,10-12,18-36,43-45 and 48-56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9,13-16,40-42,46,47 and 57-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-16,18-36 and 40-62* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. The amendment filed January 16, 2002 in Paper No. 12 is acknowledged and has been entered. Claims 17 and 37-39 have been canceled. Claims 9 and 13-16 have been amended. Claims 57-62 have been added.

2. Claims 1-16, 18-36, and 40-62 are pending in the application. Claims 1-8, 10-12, 18-36, 43-45, and 48-56 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim. Applicants timely traversed the restriction requirement in Paper No. 8.

3. Claims 9, 13-16, 40-42, 46, 47, and 57-62 are currently under prosecution.

Oath/Declaration

4. In the previous Office Action mailed July 16, 2001 (Paper No. 10), it was stated that the declaration filed with the application is defective and accordingly a substitute declaration in compliance with 37 CFR § 1.67(a) identifying this application by application number and filing date was required.

In reply, Applicants have submitted a substitute declaration that is compliant with 37 CFR §1.67(a). Therefore, the objection to the application is withdrawn.

Claim Objections Withdrawn

5. In the previous Office Action mailed July 16, 2001, claim 39 was objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

In reply, Applicants have canceled claim 39; thus, the objection to claim 39 is moot and therefore it is withdrawn.

6. In the previous Office Action mailed July 16, 2001, claims 9, 13-17, 37-42, 46, and 47 were objected to because the claims are drawn in the alternative to non-elected inventions.

In reply, Applicants have amended claims 9 and 13-16 to render the basis of the objection to the claims moot; therefore, the objection is withdrawn.

Grounds of Claim Rejections Withdrawn

Claim Rejections - 35 USC § 112

7. For the reason stated in section 10 of the previous Office Action mailed July 16, 2001 (Paper No. 10), claims 16, 17, and 37-39 were rejected under 35 U.S.C. 112, first paragraph. In reply to the Office Action, Applicants have canceled claims 17 and 37-39; thus, the rejection of claims 17 and 37-39 is rendered moot. Furthermore, Applicants have amended claim 16 to obviate the basis of the rejection. Presently claim 16 is drawn to an isolated polypeptide that is encoded by a nucleic acid molecule comprising the polynucleotide sequence set forth in SEQ ID NO: 4 or by a nucleic acid molecule comprising a polynucleotide sequence that encodes the polypeptide of SEQ ID NO: 5. As stated in the previous Office Action, the guidance, direction, and exemplification disclosed in the specification would be reasonably enabling of claims drawn to a polypeptide having the amino acid sequence set forth in SEQ ID NO: 5, which is encoded by the polynucleotide sequence set forth in SEQ ID NO: 4. Therefore, the rejection of claims 16, 17, and 37-39 under 35 USC § 112, first paragraph for the reasons stated in section 10 of the previous Office Action is withdrawn.

8. In the previous Office Action mailed July 16, 2001, claims 37-39 and 46 were rejected under 35 USC § 112, first paragraph for the reasons stated in section 11. In reply to the Office Action, Applicants have canceled claims 37-39, thus rendering the rejection of claims 37-39 moot. Furthermore, Applicants have traversed the rejection of claim 46 arguing that the specification teaches that the claimed invention can be used in ways other than in formulating a pharmaceutical composition, which in turn would be used therapeutically. Specifically, Applicants note that the specification discloses that

fusion polypeptides comprising a Secs-1 polypeptide fused to a heterologous polypeptide can be used in detecting and isolating the fusion polypeptides. This argument is not entirely persuasive, because one could argue that that any invention, which is a protein, for example, can be used in detecting the invention; therefore the argument seems contrived. Also, the skilled artisan would not make the invention, i.e., the fusion polypeptide, for the purpose of isolating the invention; in other words, the suggestion that the invention can be used to isolate the invention is paradoxical. Nevertheless, the skilled artisan could reasonably extrapolate the teachings of the specification to use the claimed invention in studying the biologic function of a Secs-1 polypeptide, since fusion polypeptides comprising, for example, a heterologous epitope are routinely used to tag polypeptides to provide a means for co-immunoprecipitating other polypeptides that associate with the polypeptides *in vivo*. Therefore, upon consideration of Applicants' arguments and review of the teachings of the specification, the rejection of claim 46 under 35 USC § 112, first paragraph for the reasons stated in section 11 of the previous Office Action is withdrawn.

9. In the previous Office Action mailed July 16, 2001, claims 14, 16, 17, and 37-39 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons stated in section 12.

In reply to the previous Office Action, Applicants have canceled claims 17 and 37-39; thus, the rejection of claims 17 and 37-39 is rendered moot. Furthermore, Applicants have amended claim 14. Presently claim 14 is drawn to an isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 6 or a fragment of the amino acid sequence set forth in SEQ ID NO: 5, or which comprises an amino acid sequence for an ortholog of SEQ ID NO: 5. Since the written description includes SEQ ID NO: 6, SEQ ID NO: 5, and SEQ ID NO: 2, which is an amino acid sequence of an ortholog of SEQ ID NO: 5, the adequacy of the written description is reasonably commensurate with the breadth of the subject matter claimed in claim 14.

Claim 16 is presently drawn to an isolated polypeptide encoded by a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 4, the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-1755, or a nucleotide sequence encoding the polypeptide of SEQ ID NO: 5. Since the written description includes SEQ ID NO: 8, which sets forth the polynucleotide sequence of a genomic DNA isolate, i.e., the gene, encoding the human Secs-1 polypeptide, the written description includes a description of a nucleotide sequence encoding the polypeptide of SEQ ID NO: 5. Therefore, since the written description also includes SEQ ID NO: 4, the adequacy of the written description is reasonably commensurate with the breadth of the subject matter claimed in claim 16. Accordingly, the rejection of claims 14, 16, 17, and 37-39 under 35 USC § 112, first paragraph for the reasons stated in section 12 of the previous Office Action is withdrawn.

10. In the previous Office Action mailed July 16, 2001, claims 9, 16, and 17 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons stated in section 14.

Applicants have canceled claim 17 in the amendment filed January 16, 2002; therefore, the grounds of rejection of claim 17 have been rendered moot.

Claims 9 and 16 were stated to be indefinite because claim 1, from which claims 9 and 16 depend, recited the phrase "hybridizes under moderately or highly stringent conditions". Applicants have amended claims 9 and 16. Presently claims 9 and 16 are independent claims and do not recite the phrase "hybridizes under moderately or highly stringent conditions". Thus, Applicants' amendment to claims 9 and 16 has obviated this ground of rejection.

Therefore, the grounds of rejection of claims 9, 16, and 17 under 35 USC § 112, second paragraph for the reasons stated in paragraphs 4-6 of section 14 of the previous Office Action are withdrawn.

Grounds of Claim Rejections Maintained and Response to Applicants' Remarks
Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 9, 14, 15, 40-42, 46, 47, and 57-62 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated polypeptide consisting of the amino acid sequence set forth in SEQ ID NO: 5 or a fragment thereof and enabling for an isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 5 does not reasonably provide enablement for any other isolated polypeptide encompassed by the claims for the reason stated in section 10 of the previous Office Action mailed July 16, 2001 (Paper No. 10). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

For clarification of the record, a typographical error was made in the previous Office Action. In section 10, paragraph 6, the fifth sentence should have read, "[t]hese polypeptides will necessarily differ from SEQ ID NO: 5 in amino acid sequence at about 30 out of every *100* positions" (italics added for emphasis).

As stated in the previous Office Action, the breadth of the claims actually encompasses any and all polypeptides. For example, claim 9 is drawn to a polypeptide produced by a process comprising culturing a host cell containing a vector comprising a polynucleotide sequence having a nucleic acid sequence as set forth in SEQ ID NO: 4, or as occurring in the DNA insert of ATCC Deposit No. PTA-1775, or which encodes a polypeptide having an amino acid sequence as set forth in SEQ ID NO: 5. Claim 9 is not limited to the polypeptide encoded by the polynucleotide sequence of SEQ ID NO: 4, as the claim only requires the vector encoding the polypeptide to comprise a polynucleotide sequence of SEQ ID NO: 4. Claim 9, therefore, encompasses any polypeptide produced by a process of culturing a host cell containing a vector encoding

the polypeptide, wherein said vector comprises at least two contiguous residues of the polynucleotide sequence set forth in SEQ ID NO: 4. Also, claim 9 encompasses any polypeptide encoded by any subsequence of the vector, not necessarily the polypeptide encoded by a polynucleotide sequence comprising a portion of SEQ ID NO: 4. Since claim 9 does not require the polynucleotide sequence encoding the claimed polypeptides to have any more than two contiguous nucleotides in common with the polynucleotide sequence set forth in SEQ ID NO: 4, claim 9 encompasses virtually every polypeptide. Furthermore, claim 9 is not limited to the polypeptide having the amino acid sequence set forth in SEQ ID NO: 5, as the claim only requires the claimed polypeptide to be encoded by a nucleic acid sequence that encodes a polypeptide, which has an amino acid sequence of the amino acid sequence set forth in SEQ ID NO: 5. Claim 9, therefore, encompasses any polypeptide produced by a process comprising culturing a host cell containing a vector comprising a polynucleotide sequence that encodes a polypeptide comprising at least two contiguous amino acids of the amino acid sequence of SEQ ID NO: 5. Since claim 9 does not require the polynucleotide sequence encoding the claimed polypeptides to encode a polypeptide having any more than two contiguous amino acids in common with the amino acid sequence set forth in SEQ ID NO: 5, the claimed polypeptides are not required to have any more than two contiguous amino acids in common with the amino acid sequence set forth in SEQ ID NO: 5 and therefore claim 9 encompasses virtually every polypeptide. Claim 14 only requires the claimed polypeptides to comprise an amino acid sequence of an ortholog of the polypeptide of SEQ ID NO: 5; therefore, claim 14 encompasses virtually every polypeptide, since any polypeptide having an amino acid sequence comprising at least two contiguous amino acids of the amino acid sequence of an ortholog of the polypeptide of SEQ ID NO: 5 is encompassed by the claim. Since any number of modifications, including substitutions and truncations, would be permitted, claim 15 encompasses any polypeptide that shares any one activity of the polypeptide, which has the amino acid sequence set forth in SEQ ID NO: 5. Virtually every polypeptide will have an activity shared by the polypeptide of SEQ ID NO: 5; for example, virtually every polypeptide of at least about five amino acids in length will be immunogenic. Therefore,

claim 15 encompasses virtually every polypeptide, except for the polypeptide of SEQ ID NO: 5, provided that the polypeptide is immunogenic or shares some other activity attributed to the polypeptide of SEQ ID NO: 5. Claims 58-60 and 62 are similarly drawn to virtually every polypeptide, except for the polypeptide of SEQ ID NO: 5, provided that the polypeptide is immunogenic or shares some other activity attributed to the polypeptide of SEQ ID NO: 5, because claims 58 and 62 also permit the polypeptide to comprise an amino acid sequence that might be acquired by any number of modifications of SEQ ID NO: 5. Finally, claims 57 and 59-61 encompass virtually every polypeptide because claims 57 and 61 only require the polypeptides encompassed by the claims to be encoded by a nucleic acid sequence comprising a region of the polynucleotide sequence set forth in SEQ ID NO: 4, provided that nucleic acid molecule of which said nucleic acid sequence is comprised encodes a polypeptide of at least twenty-five amino acids, which is not necessarily the same at the claimed polypeptide, but must have at least an activity in common with the polypeptide of SEQ ID NO: 5. Therefore, claims 57 and 59-61 encompass the vast majority of polypeptides, if not virtually every polypeptide. Clearly the teachings of the specification cannot be extrapolated to the enablement of claims with such breadth.

However, more narrowly interpreted, the claims encompass variants of the Secs-1 polypeptide, which differ in amino acid sequence from the polypeptide sequence of SEQ ID NO: 5. For example, claim 15 encompasses a polypeptide that differs from SEQ ID NO: 5 at only one position by the conservative substitution of one amino acid for another, which has chemical properties similar to the one that is replaced. However, as evidenced by the teachings of Bowie, Lazar, et al, and Burgess, et al, the skilled artisan cannot accurately predict the inherent effects of dissimilarity in the amino acid sequences of polypeptides upon protein structure and function. It is apparent that even a single amino acid substitution could often dramatically affect the biological activity and the structure-function characteristics of a protein. Therefore, it is clear that one skilled in the art cannot immediately conclude that any of the claimed variants of the Secs-1 polypeptide will have an activity, including antigenicity, that is identical or even similar to the Secs-1 polypeptide of SEQ ID NO: 5. Moreover, since the physiologic activity of the

Secs-1 polypeptide is not disclosed in the specification, apart from teaching methods for determining the activities of the claimed polypeptides that are obviously characteristic of all polypeptides (e.g., immunogenicity), the specification does not enable the use of claimed polypeptides, because one skilled in the art would not be able to determine which polypeptide are encompassed by the claims, or whether a given polypeptide encompassed by the claims can be used in accordance with the utilities of the invention, which are asserted in the specification.

In reply to the Office Action mailed July 16, 2001, Applicants have traversed these grounds of rejection under 35 USC § 112, first paragraph arguing that since the claims have been amended to delete "the objected-to limitation of 'at least about 70% identical' from the pending claims" (page 5, paragraph 2), the grounds of rejection stated in the previous Office Action have been overcome. Applicants also argue contrary to the position taken in the previous Office Action, "the breadth of the claims does not encompass any and all isolated polypeptides" (page 5, paragraph 2). Applicants have further asserted, "as the Examiner notes, Bowie et al. teach that even regions critical to the three-dimensional structure/function relationship can tolerate conservative substitutions" (page 5, paragraph 3). Applicants have opined, "provision of particular species of these types of substitutions [i.e., conservative substitutions] do not entail undue experimentation, since one of ordinary skill in the art would expect that the purportedly critical structure/activity relationship would be retained in such species" (paragraph bridging page 5 and 6).

In response to Applicants' arguments, the previous Office Action did not state, as Applicants have asserted, Bowie teaches that even regions critical to the three-dimensional structure/function relationship can tolerate conservative substitutions. Actually, the previous Office Action stated that Bowie teaches, "[c]ertain positions in the sequence are critical to the three-dimensional structure/function relationship and these regions can tolerate only conservative substitutions **or none at all**" (emphasis added) (page 6, paragraph 2). Contrary to Applicants' assertions, one skilled in the art cannot predict the effect of an amino acid substitution in an amino acid sequence of a protein upon the activity of the protein. For emphasis, it is again noted that Lazar, et al teaches

that even the conservative substitution of aspartic acid for glutamic acid causes a substantial loss of the protein's activity. Based upon the teachings of Bowie, et al, Burgess, et al, and Lazar, et al, one skilled in the art could not predict whether the broadly claimed polypeptides that have an amino acid sequence that is less than 100% identical to SEQ ID NO: 5 will function or can be used in accordance with the disclosed utilities, which the claimed invention is asserted to have. Furthermore, the specification fails to teach which amino acid residues are critical to the function of the polypeptides encompassed by the claims, or which amino acid residues might replace these critical residues without abolishing the activity of the polypeptides. Moreover, because the physiologic activity of the Secs-1 polypeptide is not disclosed in the specification and neither are the biologic functions of the other polypeptides encompassed by the claims, one skilled in the art could not make or use the claimed invention with a reasonable expectation of success without first embarking upon a course of undue experimentation to first determine which, if any specific activities the claimed polypeptide of SEQ ID NO: 5 may have, which are unique and inherently characteristic of a protein of its structure, and then to determine which, if any of the other polypeptides encompassed by the claims, which differ in structure from the Secs-1 polypeptide of SEQ ID NO: 5, retain enough structural similarity to the Secs-1 polypeptide of SEQ ID NO: 5 to share any one of its specific activities.

Additionally, it appears that Applicants have provided no factual evidence that would support their assertion that "provision of particular species of these types of substitutions [i.e., conservative substitutions] do not entail undue experimentation" or that "one of ordinary skill in the art would expect that the purportedly critical structure/activity relationship would be retained in such species". Contrary to Applicants' assertion, the disclosure of a list of amino acids, which can conservatively replace particular amino acids, does not reduce the experimentation that would be required by the skilled artisan to determine which, if any of the conservative amino acid substitutions can be made in the amino acid sequence of SEQ ID NO: 5 without abolishing any one activity of the polypeptide of SEQ ID NO: 5. Moreover, the lists of the amino acids having similar chemical properties to a particular amino acid, which

delineate the amino acids considered to be conservative replacements for the particular amino acid, are well known in the art. Nonetheless, contrary to Applicants' assertion, the knowledge of which amino acids can be used as conservative replacements for a particular amino acid does not substantially ease the experimental burden that would be placed on the practitioner of the claimed invention, when given only the benefit of the instant disclosure. According to the teachings of Bowie, Lazar, et al, and Burgess, et al, the skilled artisan would not necessarily expect a conservative amino acid substitution in the amino acid sequence of the polypeptide of SEQ ID NO: 5 to be tolerated; nor can the skilled artisan predict whether the amino acid replacement will be tolerated, since there are examples in which even conservative amino acid substitutions are not tolerated. Furthermore, the specification does not provide sufficient guidance or direction or exemplification to enable the skilled artisan to immediately know which amino acid residues are important to the activity or function of the polypeptide of SEQ ID NO: 5, and the skilled artisan could not know or predict at which positions conservative amino acid substitutions in the polypeptide sequence might be made without adversely affecting the activity or function of the polypeptides encompassed by the claims.

In summary, the deletion of the limitation requiring the claimed polypeptide to have an amino acid sequence that is only at least about 70% identical to the amino acid sequence set forth in SEQ ID NO: 5 has partially obviated the basis of the rejection. However, contrary to Applicants' assertion, the claims do encompass virtually every protein; an explanation for this broad interpretation of the claims has been provided in the paragraphs above. In this regard, it is evident that the teachings of the specification are not reasonably commensurate in scope with the claims. Nevertheless, to the extent that the claims encompass only polypeptides comprising an amino acid sequence that is nearly identical to the amino acid sequence of SEQ ID NO: 5, because one skilled in the art cannot predict whether these polypeptides can be used in the context of those applications disclosed in the specification for which the polypeptide of SEQ ID NO: 5 is asserted to have utility, one skilled in the art could not make and use the claimed invention with a reasonable expectation of success without need to perform undue

experimentation. Therefore, Applicants' arguments have been carefully considered but not found persuasive and the rejection of claims 9, 14, 15, 40-42, 46, 47, and 57-62 under 35 USC § 112, first paragraph for the reasons stated in section 10 of the previous Office Action is maintained.

For clarity of record, the rejection of claim 16 under 35 USC § 112, first paragraph has not been maintained, because as explained above, claim 16 is presently drawn to an isolated polypeptide that is encoded by a nucleic acid molecule comprising the polynucleotide sequence set forth in SEQ ID NO: 4 or by a nucleic acid molecule comprising a polynucleotide sequence that encodes the polypeptide of SEQ ID NO: 5. Therefore, unlike the other claims, the scope of claim 16 is limited to polypeptides consisting of, or comprising the amino acid sequence of SEQ ID NO: 5.

13. Claims 40-42 and 47 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons stated in section 11 of the previous Office Action mailed January 16, 2002.

While claims 40-42, 46, and 47 are specifically drawn to a derivatized polypeptide, which comprises an amino acid sequence or a fragment thereof that is at least about 70% identical to the amino acid sequence set forth in SEQ ID NO: 5, the specification teaches that the chemically derivatized polypeptides are to be used to therapeutically. For the reasons stated in the previous Office Action, the teachings of the specification cannot be extrapolated to the enablement of the invention commensurate in scope with the claims.

In reply to the previous Office Action, Applicants have canceled claims 37-39, which were specifically drawn to pharmaceutical compositions. Thus, to the extent that the rejection applied to claims 37-39, the rejection has been rendered moot. Applicants traverse the rejection of claims 40-42, 46, and 47 under 35 USC § 112, first paragraph for the reasons stated in section 11 of the previous Office Action. Applicants argue that the specification teaches that apart from its use in the manufacture of a pharmaceutical

composition, the invention of claims 40-42, 46, and 47 has other uses. In particular, Applicants refer to a disclosure on page 26, which Applicants assert indicates that a Secs-1 polypeptide fused to a heterologous polypeptide, such as an epitope, can be used in detecting or isolating a Secs-1 polypeptide. Also, Applicants point to a disclosure on page 57, which Applicants assert indicates that the claimed derivatives of a Secs-1 polypeptide may be prepared by chemically coupling a Secs-1 polypeptide to biotin, for example, and then the biotinylated derivative of a Secs-1 polypeptide can be used to isolate a Secs-1 polypeptide. Applicants contend that these disclosures provide sufficient guidance and direction to enable the skilled artisan to make and use the claimed invention.

In response to Applicants' arguments, it is first necessary to clarify a statement that was made in the previous Office Action. In the previous Office Action, in section 11, paragraph 2, it was stated, "claims 40-42, 46, and 47 are specifically drawn to a derivatized or fusion polypeptide". However, it is noted that the term "Secs-1 polypeptide derivatives" is defined as polypeptides "that have been chemically modified" (page 12, lines 21-27). Therefore, claims 40-42 are drawn to chemical derivatized polypeptides, not fusion polypeptides. On the other hand, claims 46 and 47 are drawn to fusion polypeptides, not derivatives of polypeptides. Claim 47 is specifically drawn to a fusion polypeptide comprising a Secs-1 polypeptide fused to an IgG constant domain or fragment thereof.

Applicants argue that the claimed derivatives of polypeptides and the claimed fusion polypeptides have uses other than in formulating pharmaceutical compositions. However, contrary to Applicants' arguments, it does not appear that the specification teaches any other use of chemically modified derivative of a Secs-1 polypeptide. While the specification teaches a Secs-1 polypeptide fused to an epitope can be used in detecting or isolating the fusion protein, the specification does not explicitly teach any use other than in formulating a pharmaceutical composition, for the claimed fusion polypeptide comprising a Secs-1 polypeptide fused to an IgG constant domain or fragment thereof (claim 47). Furthermore, while the specification discloses that a Secs-1 polypeptide can be biotinylated, as Applicants have noted, the specification teaches

that the biotinylated Secs-1 polypeptide is used to formulate a pharmaceutical composition (page 57, paragraph following the paragraph to which Applicants have referred). There does not appear to be any disclosure suggesting that the claimed derivatives of a Secs-1 polypeptide can be used in isolating a Secs-1 polypeptide, as Applicants have contended. Moreover, although the skilled artisan could isolate a biotinylated Secs-1 polypeptide, contrary to Applicants' assertion, the skilled artisan would not be motivated to derivatize a Secs-1 polypeptide by biotinylation in order to isolate the polypeptide, since the polypeptide would necessarily have to have been isolated so that it could be biotinylated.

Consequently, Applicants' arguments have been carefully considered. With regard to claim 46, as noted above, the arguments are persuasive; however, with regard to claims 40-42 and 47, the arguments have not been found persuasive. Therefore, the rejection of claims 4-42 and 47 under 35 USC § 112, first paragraph for the reasons stated in section 11 of the previous Office Action is maintained.

14. Claims 9, 15, 40-42, 46, 47, and 57-62 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 9, 15, 40-42, 46, 47, and 57-62 are drawn a very broad genus of polypeptides. Although a polypeptide consisting of, or comprising the amino acid sequence set forth in SEQ ID NO: 5 and a polypeptide that is encoded by a nucleic acid molecule consisting of, or comprising the polynucleotide sequence set forth in SEQ ID NO: 4 is encompassed by claims 9, 57, and 59-61, these claims also encompass polypeptides comprising only portions, i.e., an amino acid sequence, of the amino acid sequence set forth in SEQ ID NO: 5 and/or polypeptides encoded by nucleic acid molecules comprising a polynucleotide sequence that contains only a portion, or region of the polynucleotide sequence set forth in SEQ ID NO: 4. Since claims 15, 58, and 62 permit the claimed polypeptide to have an amino acid sequence in which any number of

amino acid substitutions and/or truncations of the amino acid sequence of SEQ ID NO: 5 have been made, the claims only limit the claimed polypeptides to those having an activity of the polypeptide of SEQ ID NO: 5, such as immunogenicity or sensitivity to a protease. In fact, as stated in the 35 USC § 112, first paragraph rejection above (section 11), claims 9, 15, 40-42, 46, 47, and 57-62 encompass the vast majority of polypeptides.

Furthermore, while claims 15, 40-42, 46, 47, 58, 59, 60, and 62 encompass recombinant polypeptides, which are encoded by nucleic acid molecules engineered to encode polypeptides having the amino acid sequence set forth in SEQ ID NO: 5, albeit with one or more conservative amino acid substitutions or a truncation, the claims also encompass naturally occurring polypeptides, which are encoded by allelic variants of the gene encoding the amino acid sequence of SEQ ID NO: 5. These naturally occurring polypeptides may differ in structure from the polypeptide of SEQ ID NO: 5 by the inclusion of one or more amino acid substitutions resulting from the presence of a polymorphism or mutation in the polynucleotide sequence of the gene encoding the polypeptide. The claims also encompass naturally occurring splice variants of the polypeptide of SEQ ID NO: 5, which are encoded by messenger RNA (mRNA) molecules that have been alternatively spliced. These naturally occurring polypeptides may differ in structure from the polypeptide of SEQ ID NO: 5 by truncation of, or a deletion or an insertion in their amino acid sequences.

Of course, since the claims are drawn to a vast genus of polypeptides, it is evident that the written description is not reasonably commensurate with the breadth of the claims. Nevertheless, since the claims also encompass polypeptides encoded by allelic variants or alternatively spliced mRNA molecules, the disclosure of two members of the claimed genus of polypeptides, namely SEQ ID NO: 2 and 5 is considered insufficient to meet the written description requirement of 35 USC § 112, first paragraph, because the structures of the two species of polypeptides is not sufficiently representative of claimed genus. The structures and amino acid sequences of the vast majority of members of the genus of polypeptides encompassed by the claims are not disclosed in the specification, nor are the vast majority of the structures and

polynucleotide sequences of the nucleic acid molecules encoding the claimed polypeptides disclosed. One skilled in the art cannot determine the structure or the polynucleotide sequence of a reasonable number of the nucleic acid molecules, which encode the claimed polypeptides, based only upon the disclosure of the polynucleotide sequences of two cDNA molecules, namely SEQ ID NO: 1 and SEQ ID NO: 4, which encode the polypeptides of SEQ ID NO: 2 and SEQ ID NO: 5, respectively, and the polynucleotide sequence of a genomic isolated, namely SEQ ID NO: 8, which apparently also encodes the polypeptide of SEQ ID NO: 5. In particular, the skilled artisan could not determine the structure of a gene encoding an allelic variant of the polypeptide of SEQ ID NO: 5; the structural details of a gene can only be determined empirically. Also, the skilled artisan could not determine the structure of the alternatively spliced mRNA molecule encoding the splice variant of the polypeptide of SEQ ID NO: 5; again, the structural details of an alternatively spliced mRNA can only be determined empirically.

Thus, the skilled artisan could not immediately envision a representative number of members of the claimed genus of polypeptides, or a representative number of the nucleic acid molecules that encode the claimed polypeptides. For example, the skilled artisan could not immediately envision the detailed structure of a polypeptide, i.e., its amino acid sequence, which is encoded by an allelic variant of the gene, which encoded the mRNA from which the cDNA of SEQ ID NO: 4 was derived. In accordance, the claimed subject matter is not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time the application was filed.

Furthermore, the skilled artisan could not instantly recognize a reasonably representative number of members of the claimed genus of polypeptides, because the skilled artisan could not immediately recognize a reasonably representative number of nucleic acid molecules that encode the claimed polypeptides. Apart from the describing the amino acid sequence of the polypeptide of SEQ ID NO: 5, the specification fails to set forth a written description of the common features shared by the members of the claimed genus of polypeptides, which if presented, would have delineated the claimed

genus of polypeptides by serving to provide a description of the features that distinguish members of the genus from other polypeptides, which are not encompassed by the claims. For example, the specification fails to describe the amino acid residues that are conserved at various positions throughout the amino acid sequences of the polypeptides, which would most likely be the amino acids critical to conformation and function of the polypeptides. As another example, the specification fails to set forth a common activity or function, which each member of the claimed genus of polypeptides has, but even if the claims recited a limitation requiring the claimed polypeptides to have a specific activity or function, because the specification fails to describe which amino acids are critical for retention of such an activity or function, the recitation of the limitation would only serve to describe what the members of the claimed genus of polypeptides must do, rather than what they are.

Adequate written description requires more than a mere statement that it is part of the invention. The polynucleotide sequences of the nucleic acid molecules encoding the polypeptides or the amino acid sequences of the polypeptides themselves are required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. With the exception of SEQ ID NO: 5, the skilled artisan cannot immediately envision the detailed structure of the naturally occurring polypeptides that are encompassed by the claims. Consequently, the disclosure is insufficient to meet the written description requirement of 35 USC 112, first paragraph.

In reply to the previous Office Action, Applicants have traversed the rejection of claims 9, 14-17, 37-42, 46, and 47 under 35 USC § 112, first paragraph for the reasons stated in section 12. Applicants have canceled claims 17 and 37-39, which renders the rejection of claims 17 and 37-39 moot. With respect to claims 9, 14-16, 40-42, 46, and 47, Applicants argue that the written description is sufficient to meet the requirements of 35 USC § 112, first paragraph. Since the present claims do not recite a limitation requiring the claimed polypeptide to be encoded by an allelic variant or a splice variant of the gene, which encoded the mRNA molecule from which the cDNA of SEQ ID NO: 4 was derived, Applicants imply it is not necessary that the disclosure include a written

description of an allelic variant or splice variant of the polypeptide of SEQ ID NO: 5, or a written description of the gene encoding the allelic variant or splice variant.

In response to Applicants' argument, however, presently claims 15, 40-42, 46, 47, 58, 59, 60, and 62 encompass polypeptides, which are allelic variants or splice variants of the polypeptide of SEQ ID NO: 5. Furthermore, the present claims encompass naturally occurring polypeptides encoded by alleles of the gene that encoded the mRNA from which the cDNA of SEQ ID NO: 4 was derived. Although the amino acid sequence of the polypeptide of SEQ ID NO: 5 could be instantly envisioned, given the benefit of the disclosure, the skilled artisan could not immediately envision the detailed structure, or recognize the genes that encode the allelic variants of the polypeptide of SEQ ID NO: 5. Also, again, claims 9, 15, 40-42, 46, 47, and 57-62 encompass the vast majority of polypeptides. For the reasons stated in the previous Office Action and reiterated above, the disclosure is not sufficient to meet the written description requirement of 35 USC § 112, first paragraph and Applicants' arguments have been carefully considered, but have not been found persuasive. Therefore, the rejection of claims 9, 15, 40-42, 46, and 47 under 35 USC § 112, first paragraph for the reasons stated in section 12 of the previous Office Action is maintained. For the same reasons, claims 57-62, which were added by the amendment filed January 16, 2002, are also rejected under 35 USC § 112, first paragraph.

Amending limitation (iii) of claim 9 to read, "that encodes a polypeptide having *the* amino acid sequence set forth in SEQ ID NO. 5" (italics added for emphasis) can obviate the grounds of this rejection of claim 9, because the claim would then only encompass a polypeptide encoded by a nucleic acid molecule encoding the amino acid sequence set forth in SEQ ID NO: 5, and not virtually every polypeptide, which is encoded by a nucleic acid molecule encoding only a portion of the sequence set forth in SEQ ID NO: 5. Amending claims 15, 58, and 62 to recite, for example, "non-naturally occurring" before "polypeptide" in line 1 of claim 15, before "polypeptide" in line 3 of claim 58, and before "polypeptide" in line 2 of claim 62, together with amending the claim to recite a limitation requiring the claimed polypeptides to have a specific activity, which is particularly characteristic of the polypeptide of SEQ ID NO: 5 and could be

used to distinguish members of the claimed genus of polypeptide from other polypeptides, can obviate these grounds of rejection of claims 15, 40-42, 46, 47, 58, and 62. Support for recitation of the term "non-naturally occurring" is found in the specification (page 14, lines 20-22). Amending claims 57 and 61 to delete the phrase "a nucleotide sequence of a region of" after "having" in line 2 of claim 57 and after "comprising" in line 1 of claim 61 and also amending claims 57 and 61 to delete the phrase "a region of" after "or" in line 3 of claim 57 and after "or" in line 2 of claim 61 can obviate the grounds of this rejection of claims 57 and 61.

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 9, 13-16, 40-42, 46, 47, and 57-62 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons stated in section 14 of the previous Office Action mailed July 16, 2001.

(a) Claims 14-16, 37-42, 46, 47, and 57-62 are vague and indefinite because claims 14-16, 57, 58, 61, and 62 recite the phrase "has an activity". As stated in the previous Office Action, recitation of the phrase renders the claims vague and indefinite because it is unclear to which activity the claims refer and therefore it cannot be ascertained which activity of the polypeptide of SEQ ID NO: 5 the claims require the claimed polypeptides to have. Accordingly, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the claimed invention. Moreover, since it is unclear to which activity the claims refer, it is unclear how one of ordinary skill in the art could possibly determine the activity of any a particular polypeptide and therefore it is unclear how one can determine the metes and bounds of the claims, which would serve to delineate the particular subject matter which Applicants regard as their invention.

Applicants traverse the rejection arguing, "claims containing this limitation encompass only those Secs-1 polypeptide variants that possess an inherent activity of the polypeptide set forth in SEQ ID NO: 5". Applicants assert, "in view of the inherency of activity that resides in polypeptides having the amino acid sequence as set forth in SEQ ID NO: 5, [...] the term ["activity"] is not indefinite" (page 7, paragraph 2).

In response to Applicants' arguments, if Applicants regard an isolated polypeptide having the inherent activity of the polypeptide of SEQ ID NO: 5, then the claims should recite a limitation requiring the claimed polypeptides to have the inherent activity of the polypeptide of SEQ ID NO: 5. As the claims read presently, however, the isolated polypeptides are merely required to have one of the activities of the polypeptide of SEQ ID NO: 5, and notably the claims fail to particularly point to the distinct activity that the claimed polypeptides are required to have. Accordingly, for the reasons stated in the previous Office Action and reiterated here in this Office Action, recitation of the phrase "has an activity" renders the claims both vague and indefinite, because the subject matter that Applicants regard as their invention is not clearly delineated. Because the claim is vague and indefinite, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention, particularly since as noted in the rejections under 35 USC § 112, first paragraph, the specification does not teach which distinct activities the polypeptide of SEQ ID NO: 5 has. Therefore, Applicants' arguments have been carefully considered but not found persuasive.

As a suggestion, Applicants may wish to consider deleting the limitation requiring the polypeptide of claim to have an activity of the polypeptide having the amino acid sequence set forth in SEQ ID NO: 5. The limitation does not further limit the subject matter of the claims, if, as Applicants have argued, the activity of the claimed polypeptides is an inherent feature of those polypeptides.

(b) Claims 9, 13, 16, 40-42, 46, 47, 57, and 59-61 are indefinite because claims 9, 13, 16, 57, and 61 recite the phrase "the DNA insert in ATCC Deposit No. PTA-1755". As stated in the previous Office Action, recitation of the phrase renders the claims indefinite because it is not clear to which DNA insert the claims refer and accordingly

one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

Applicants traverse the rejection arguing that the amendment to the claims has obviated this ground of rejection.

In response to Applicants' arguments, the amendment has not obviated this ground of rejection. As stated in the previous Office Action, recitation of the phrase renders the claims indefinite because it is unclear to which DNA insert the claims refer. Furthermore, it does not appear that the specification defines the DNA insert of ATCC Deposit No. PTA-1755; moreover, it does not appear that the specification adequately defines the material that is deposited. The specification refers to the deposited material on page 85, lines 11-15. *Presumably*, the deposited material is a host cell transformed with a plasmid. P*resumably*, the plasmid is p7T73D, although the specification does not clearly indicate which of the two plasmids listed was used in cloning the cDNA molecule encoding the human Secs-1 polypeptide. Evidently, the plasmid contains an insert, since the claim requires the deposited material to contain an insert. However, it is not absolutely evident that the cDNA molecule encoding the polypeptide of SEQ ID NO: 5 is the DNA insert to which the claims refer, or if the DNA insert to which the claims refer has the polynucleotide sequence set forth in SEQ ID NO: 4. Accordingly, the claims are indefinite because it cannot be ascertained with the required and necessary certainty, to which DNA insert the claims refer. Plasmids routinely have more than one insert. For these reasons, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. Therefore, Applicants' argument has been carefully considered but not found persuasive.

As suggested in the previous Office Action, amending claims 9, 13, 16, 57, and 61 to recite, for example, the phrase "wherein said insert comprises a polynucleotide sequence that encodes the amino acid sequence set forth in SEQ ID NO: 5" can obviate this rejection. However, a better suggestion would be to amend claims 9, 13, 16, 57, and 61 to recite the limitation, "wherein said insert comprises the polynucleotide sequence set forth in SEQ ID NO: 4", as this would obviate this ground of rejection

under 35 USC § 112, second paragraph without raising a written description issue under § 112, first paragraph.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 9, 13, 14, 16, 57, and 59-61 are rejected under 35 U.S.C. 102(a) as being anticipated by The FAPESP/LICR Human Cancer Genome Project (GenBank EST Database Accession No. AW351839, 1999), as evidenced by a USPTO database search using SEQ ID NO: 5 as a query (see USPTO Search Report US-09-599-087-5.rst, result 1), for the reason stated in section 16 of the previous Office Action mailed July 16, 2001.

The FAPESP/LICR Human Cancer Genome Project teach the amino acid sequence of a polypeptide that is 100% identical to the amino acid sequence set forth in SEQ ID NO: 5. Because the polypeptide of the prior art has the same amino acid sequence as the claimed polypeptide, the polypeptide of the prior art will have an activity of the polypeptide of SEQ ID NO: 5.

Applicants have traversed the rejection of claims 9, 13, 14, 16, and 17 under 35 USC § 102(a) arguing, the FAPESP/LICR Human Cancer Genome Project does not teach the expressed sequence tag (EST), which is a cDNA molecule derived from a messenger RNA (mRNA) molecule that ordinarily encodes a polypeptide, encodes the amino acid sequence of a Secs-1 polypeptide. Furthermore, Applicants argue that the existence of multiple open-reading frames (ORF) suggests that the polynucleotide sequence may encode a polypeptide other than the Secs-1 polypeptide.

As Applicants have canceled claim 17 in the amendment filed January 16, 2002, the rejection of claim 17 under 35 USC § 102(a) has been rendered moot. Therefore, the rejection of claim 17 is withdrawn.

In response to Applicants' arguments, the claims presently recite a limitation that the nucleic acid molecule encoding the claimed polypeptide have a nucleotide sequence that encodes a polypeptide having an amino acid sequence as set forth in SEQ ID NO: 5. The nucleic acid molecule of the prior art has a nucleotide sequence that encodes the amino acid sequence set forth in SEQ ID NO: 5. Therefore, the prior art nucleic acid molecule is deemed to encode a polypeptide that has the same as the amino acid sequence of the polypeptide of the instant claims, absent a showing of any differences. The office does not have the facilities for examining and comparing Applicants' product with the product of the prior art in order to establish that the product encoded by the nucleic acid molecule of the prior art does not possess the same material, structural, and functional characteristics of the claimed product or would not function identically to the claimed polypeptides. In the absence of evidence to the contrary, the burden is upon the Applicants to prove that the claimed polypeptides are functionally different than those taught by the prior art and to establish patentable differences. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *Ex parte Gray*, 10 USPQ 2d 1922 1923 (PTO Board of Patent Appeals and Interferences).

Additionally, it is noted that specification only sets forth the *deduced* amino acid sequence of the human Secs-1 polypeptide in SEQ ID NO: 5 (page 8, line 2), which is merely a prediction of the amino acid sequence that might be encoded by the nucleic acid molecule of SEQ ID NO: 4 based upon an analysis of possible open-reading frames. Moreover, the specification does not teach the actual amino acid sequence of the protein or proteins encoded by the polynucleotide sequence of the cDNA molecule of SEQ ID NO: 4. In fact, apart from a general disclosure of conventional methodology that might be used to express and characterize the polypeptide encoded by the cDNA molecule of SEQ ID NO: 4, there is no indication in the specification that the polypeptide encoded by the cDNA has been expressed, or that the expressed polypeptide has a molecular weight that is consistent with the length of its predicted sequence, or that the

amino acid sequence of the polypeptide has been sequenced directly to confirm its predicted amino acid sequence.

Nevertheless, there is a reasonable presumption that the cDNA molecule of SEQ ID NO: 4 will encode the polypeptide of SEQ ID NO: 5. The longest open-reading frame, i.e., the longest run of codons, each consisting of three consecutive nucleotides, encoding an amino acid, contained in the polynucleotide sequence of a cDNA molecule is generally presumed to be the coding sequence of the cDNA molecule, or the sequence that is translated to a sequence of amino acids during biosynthesis of the polypeptide encoded by the cDNA molecule. Similarly, there is a reasonable presumption that the nucleic acid molecule of the prior art will encode a polypeptide that has the amino acid sequence set forth in SEQ ID NO: 5, because the longest open-reading frame contained by the polynucleotide sequence of the nucleic acid molecule of the prior art would encode a polypeptide having the amino acid sequence of SEQ ID NO: 5.

Applicants' arguments have been carefully considered, but have not been found persuasive. Therefore, the rejection of claims 9, 13, 14, 16 under 35 USC § 102(a) for the reason stated in section 16 of the previous Office Action is maintained. Furthermore, this same ground of rejection is now applied to claims 57 and 59-61, since the polypeptide encoded by the nucleic acid molecule of the prior art is deemed the same as the polypeptide of claims 57 and 59-61.

19. Claims 9, 14, 15, and 57-62 are rejected under 35 U.S.C. 102(b) as being anticipated by Hillier, et al (GenBank EST Database Accession No. AA422178, 1997), as evidenced by a USPTO database search using SEQ ID NO: 5 as a query (see USPTO Search Report US-09-599-087-5.rst, result 2), for the reason stated in section 17 of the previous Office Action mailed July 16, 2001.

Hillier, et al teach the amino acid sequence of a polypeptide that is at least about 70% identical to the amino acid sequence set forth in SEQ ID NO: 5. In fact, the amino acid sequence of the polypeptide that is 100% identical to the amino acid sequence set forth in SEQ ID NO: 5 over the region spanning from the amino acid at position 1 to the

amino acid at position 76. Therefore, the polypeptide of Hillier, et al is truncated at the C-terminus, encoding a fragment of SEQ ID NO: 5 comprising at least about 25 amino acid residues. Because the polypeptide of the prior art has the same amino acid sequence as the claimed polypeptide, the polypeptide of the prior art will have an activity of the polypeptide of SEQ ID NO: 5.

Applicants have traversed the rejection of claims 9 and 14-17 under 35 USC § 102(b) arguing that for the reasons already addressed in the rejection above, the prior art cited as a basis of the rejection does not anticipate the claimed invention.

In response to Applicants' arguments, as stated in reply to Applicants' traversal of the rejection above, the polypeptide of the prior art is deemed the same as the polypeptide of the instant claims, absent a showing of any difference. Although the polypeptide encoded by the nucleic acid molecule of Hillier, et al would be a truncated version of the polypeptide of SEQ ID NO: 5, the nucleic acid molecule of Hillier, et al has a nucleotide sequence that encodes a polypeptide having an amino acid sequence set forth in SEQ ID NO: 5. In fact, the nucleic acid molecule of Hillier, et al has a nucleotide sequence that encodes a polypeptide having the amino acid sequence of SEQ ID NO: 5 spanning the amino acids at positions 1 to 76 of the amino acid sequence of SEQ ID NO: 5. Furthermore, because the nucleic acid molecule of Hillier, et al encodes a polypeptide that is a truncated version of the polypeptide having the amino acid sequence set forth in SEQ ID NO: 5, the teachings of the prior meet the limitations of claims 15, 58, and 62, which require the claimed polypeptide to have the amino acid sequence set forth in SEQ ID NO: 5 with at least one modification that is truncation. Therefore, Applicants' arguments have been carefully considered but not found persuasive. The rejection of claims 9, 14, 15 under 35 USC § 102(b) for the reason stated in section 17 of the previous Office Action is maintained. Furthermore, this same ground of rejection is now applied to claims 57-62, since the polypeptide encoded by the nucleic acid molecule of the prior art is deemed the same as the polypeptide of claims 57-62.

Note that the rejection of claim 16 has been withdrawn. However, as discussed above, neither the claims nor the specification define the DNA insert to which the claims

refer; therefore, it cannot be ascertained whether the nucleic acid molecule of the prior art has the same polynucleotide sequence as the DNA insert to which the claims refer. Thus, it cannot be determined whether the polypeptide encoded by the nucleic acid molecule of Hillier, et al anticipates the claimed polypeptide.

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. Claims 9, 13, 14, 16, 17, 46, 57, and 59-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over The FAPESP/LICR Human Cancer Genome Project (GenBank EST Database Accession No. AW351839, 1999), as evidenced by a USPTO database search using SEQ ID NO: 5 as a query (see USPTO Search Report US-09-599-087-5.rst, result 1), for the reason stated in section 19 of the previous Office Action mailed July 16, 2001.

The FAPESP/LICR Human Cancer Genome Project teach that which is set forth in the 35 USC § 102(a) rejection above. However, The FAPESP/LICR Human Cancer Genome Project do not disclose a fusion polypeptide comprising the polypeptide having the amino acid sequence set forth therein fused to a heterologous amino acid sequence.

As stated in the previous Office Action, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the nucleic acid molecule of The FAPESP/LICR Human Cancer Genome Project so that the modified nucleic acid molecule would encode a fusion polypeptide comprising the polypeptide comprising the amino acid sequence of The FAPESP/LICR Human Cancer Genome Project fused to a FLAG-epitope tag, because the utility of FLAG-epitope tags

in studies of a protein's activities is well established in the art. One of ordinary skill in the art at the time the invention was made would have been motivated to modify the nucleic acid molecule of The FAPESP/LICR Human Cancer Genome Project so that the modified nucleic acid molecule would encode a fusion polypeptide comprising the polypeptide comprising the amino acid sequence of The FAPESP/LICR Human Cancer Genome Project fused to a FLAG-epitope tag, because antibodies that specifically bind the epitope tag could be used to immunoprecipitate the fusion protein, facilitating purification and other studies.

Applicants have traversed the rejection of claims 9, 13, 14, 16, 17, and 46 under 35 USC § 103(a) arguing that one of ordinary skill in the art would not have been able to modify the nucleic acid molecule of the FAPESP/LICR Human Cancer Genome Project so that the modified polypeptide encoded by the modified nucleic acid molecule of the FAPESP/LICR Human Cancer Genome Project would be a Secs-1 fusion polypeptide. Accordingly, Applicants contend that the cited prior art cannot render the claimed invention obvious under 35 USC § 103(a).

In response to Applicants' arguments, Applicants have provided no factual evidence that would support their assertion that one of ordinary skill in the art would not have been able to modify the nucleic acid molecule of the FAPESP/LICR Human Cancer Genome Project so that the modified polypeptide encoded by the modified nucleic acid molecule of the FAPESP/LICR Human Cancer Genome Project would be a Secs-1 fusion polypeptide. There appears to be no obvious reason that one of ordinary skill in the art could not have successfully modified the nucleic acid molecule of the FAPESP/LICR Human Cancer Genome Project so that the modified polypeptide encoded by the modified nucleic acid molecule of the FAPESP/LICR Human Cancer Genome Project would be a Secs-1 fusion polypeptide. Furthermore, as noted in the previous Office Action, it would have been obvious to modify the nucleic acid molecule of the FAPESP/LICR Human Cancer Genome Project so that the modified nucleic acid molecule would encode a fusion polypeptide comprising the polypeptide comprising the amino acid sequence of the FAPESP/LICR Human Cancer Genome Project fused to a FLAG-epitope tag, because the utility of FLAG-epitope tags in studies of a protein's

activities is well established in the art. Therefore, Applicants' arguments have been carefully considered but not found persuasive and the rejection of claims 9, 13, 14, 16, 17, 46, 57, and 59-61 for the reason stated in section 19 of the previous Office Action is maintained.

22. Claims 9, 14, 15, 46, and 57-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hillier, et al (GenBank EST Database Accession No. AA422178, 1997), as evidenced by a USPTO database search using SEQ ID NO: 5 as a query (see USPTO Search Report US-09-599-087-5.rst, result 2), for the reason stated in section 20 of the previous Office Action mailed July 16, 2001.

As stated in the previous Office Action, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the nucleic acid molecule of Hillier, et al so that the modified nucleic acid molecule would encode a fusion polypeptide comprising the polypeptide comprising the amino acid sequence of Hillier, et al fused to a FLAG-epitope tag, because the utility of FLAG-epitope tags in studies of a protein's activities is well established in the art. One of ordinary skill in the art at the time the invention was made would have been motivated to modify the nucleic acid molecule of Hillier, et al so that the modified nucleic acid molecule would encode a fusion polypeptide comprising the polypeptide comprising the amino acid sequence of Hillier, et al fused to a FLAG-epitope tag, because antibodies that specifically bind the epitope tag could be used to immunoprecipitate the fusion protein, facilitating purification and other studies.

Applicants have traversed the rejection of claims 9, 14-17, and 46 under 35 USC § 103(a) arguing that one of ordinary skill in the art would not have been able to modify the nucleic acid molecule of Hillier, et al so that the modified polypeptide encoded by the modified nucleic acid molecule of Hillier, et al would be a Secs-1 fusion polypeptide. Accordingly, Applicants contend that the cited prior art cannot render the claimed invention obvious under 35 USC § 103(a).

As Applicants have canceled claim 17 in the amendment filed January 16, 2002, the rejection of claim 17 under 35 USC § 103(a) has been rendered moot. Therefore, the rejection of claim 17 is withdrawn.

In response to Applicants' arguments, Applicants have provided no factual evidence that would support their assertion that one of ordinary skill in the art would not have been able to modify the nucleic acid molecule of Hillier, et al so that the modified polypeptide encoded by the modified nucleic acid molecule of Hillier, et al would be a Secs-1 fusion polypeptide. There appears to be no obvious reason that one of ordinary skill in the art could not have successfully modified the nucleic acid molecule of Hillier, et al so that the modified polypeptide encoded by the modified nucleic acid molecule of Hillier, et al would be a Secs-1 fusion polypeptide. Furthermore, as noted in the previous Office Action, it would have been obvious to modify the nucleic acid molecule of Hillier, et al so that the modified nucleic acid molecule would encode a fusion polypeptide comprising the polypeptide comprising the amino acid sequence of Hillier, et al fused to a FLAG-epitope tag, because the utility of FLAG-epitope tags in studies of a protein's activities is well established in the art. Therefore, Applicants' arguments have been carefully considered but not found persuasive and the rejection of claims 9, 14, 15, 46, and 57-62 for the reason stated in section 20 of the previous Office Action is maintained.

New Grounds of Claim Rejections

Claim Rejections – 35 USC § 112

23. Claims 57 and 59-61 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 57 and 61 recite the phrases, "a region of the nucleotide sequence of SEQ ID NO: 4" and "a region of the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-1755". However, there does not appear to be sufficient antecedent basis in the specification for recitation of the terms "a region of the nucleotide sequence of SEQ ID NO: 4" and "a region of the nucleotide sequence of the DNA insert".

Accordingly, recitation of the terms in the claims appears to introduce new matter and thereby violates the written description requirement of 35 USC § 112, first paragraph.

This issue might be resolved if Applicants will point to specific disclosures in the specification that are believed to properly support recitation of the terms in the claims.

24. Claims rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Evidence that claims 9, 15, and 57-62 fail to correspond in scope with that which Applicants regard as the invention can be found in Paper No. 12 filed January 18, 2002. In that paper, Applicants have stated, "the breadth of the claims does not encompass any and all isolated polypeptides" (page 5, paragraph 2). This statement indicates that the invention is different from what is defined in the claims because for the reasons discussed in the rejections under 35 USC § 112, first paragraph, claims 9, and 57-62 do appear to encompass virtually every polypeptide, without any overt exceptions, provided that the polypeptide is immunogenic. Claims 15, 58, and 62 also appear to encompass virtually every polypeptide with the notable exception of the polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 5, provided that the polypeptide is immunogenic. Although in their remarks, Applicants contend, "[m]any isolated polypeptides [...] lack an activity of the polypeptide set forth in SEQ ID NO: 5" (page 5, paragraph 2), an example of such a polypeptide has not been provided, and few if any, polypeptides are expected to lack immunogenicity, provided that the polypeptides are of a sufficient length to bind an immunoglobulin, MHC gene product, or a T-cell receptor. As immunogenicity is an inherent activity of the polypeptide of SEQ ID NO: 5, virtually every polypeptide of such sufficient length will necessarily have an activity of the polypeptide of SEQ ID NO: 5. Furthermore, it is noted that claim 14 in an alternative, actually requires the claimed polypeptide to be antigenic, i.e., immunogenic.

Additionally, there is evidence that claims 9, 14, and 15 fail to correspond in scope with that which Applicants regard as the invention. Again in Paper No. 12, Applicants have stated, "[the prior art] does not teach the amino acid sequence of Secs-1 polypeptide" and "[the prior art teaches a polynucleotide sequence], but does not

teach the amino acid sequence of Secs-1 polypeptide" (page 8, paragraph 5) and therefore Applicants contend that the prior art does not anticipate the claimed invention. Presumably, the amino acid sequence of Secs-1 polypeptide to which Applicants refer in their remarks is the amino acid set forth in SEQ ID NO: 5. Thus, these statements indicate that the invention is different from what is defined in the claims because the claims do not require the claimed polypeptide to be encoded by a nucleic acid molecule comprising the entire coding sequence of the amino acid sequence of SEQ ID NO: 5. Claim 9 only requires the polynucleotide sequence of the nucleic acid molecule to encode a polypeptide, which has an amino acid sequence of SEQ ID NO: 5, not which has the amino acid sequence of SEQ ID NO: 5. Claim 14 only requires the isolated polypeptide to comprise a fragment of the amino acid sequence set forth in SEQ ID NO: 5, provided the fragment is at least twenty-five amino acids and length and is immunogenic. In other words, claim 14 does not require the nucleic acid molecule encoding the claimed polypeptide to comprise the entire coding sequence of polynucleotide sequence encoding the polypeptide of SEQ ID NO: 5, but only a portion of its sequence encoding said fragment. Finally, claim 15 only requires the isolated polypeptide to comprise an amino acid sequence that differs from the amino acid sequence of SEQ ID NO: 5, provided that the polypeptide has an activity of the polypeptide of SEQ ID NO: 5, for example, is immunogenic. Claim 15 does not require the claimed polypeptide to be encoded by the polynucleotide sequence encoding the amino acid sequence of SEQ ID NO: 5; and, in fact, claim 15 requires the claimed polypeptide to be encoded by a polynucleotide sequence that differs from the polynucleotide sequence encoding the amino acid sequence set forth in SEQ ID NO: 5. Therefore, the noted remarks made by the Applicants in Paper No. 12 suggest that they regard the invention as something other than that, which is presently claimed in this application.

25. Claims 57 and 59-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 57 and 59-61 are vague and indefinite because claims 57 and 61 recite the term "a region of the nucleotide sequence of SEQ ID NO: 4" and also because claims 57 and 61 recite the term "a region of the nucleotide sequence of the DNA insert in ATCC Deposit No. PTA-1755". Recitation of the terms in the claims renders the claims vague and indefinite because it cannot be ascertained to which region of the nucleotide sequence set forth in SEQ ID NO: 4 or to which region of the nucleotide sequence of the DNA insert in the deposit, the claims refer. Accordingly, one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the claimed invention.

Conclusion

26. No claims are allowed.

27. Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

28. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (703) 305-3008. The examiner can normally be reached on Monday-Thursday, alternate Fridays, 8:00AM-5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C. Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642

slr
April 15, 2002

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600